Niobium-Zirconium alloy for medical devices or their parts

The present invention relates to a Niobium-Zirconium Alloy for medical implants or devices to be inserted into the human body for a prolonged period of time.

Background of the Invention

A medical implant or device must satisfy a number of requirements. When the material for manufacturing these devices is chosen, factors like biocompatibility and a range of mechanical properties have to be considered. The material must not cause any inflammatory reaction or allergic reaction. Commonly used materials often include nickel, like medical grade 316L stainless steel, which contains about 16% nickel. For patients with an allergic reaction the implantation of such materials is contraindicated. Another consideration in material selection is the need for the implanting physician to be able to visualize the position of the medical implant or device during procedure to the desired target site in the body, and for purposes of examination from time to time thereafter at the implant site, typically by X-ray fluoroscopy.

With the growing importance of magnetic resonance imaging (MRI), MRI compatibility is desirable. The metal alloys commonly used for implantation (like stainless steel 316) induce a local disturbance of the magnetic field used in MRI, to the extent that imaging of surrounding tissue is impeded. Although alloys like Nitinol behave more favourably in MRI, their MRI compatibility is not considered to be sufficiently good.

This invention relates to medical devices or implants in general such as catheters, guide wires, stents, stent grafts and heart valve repair devices.

Stents are generally thin walled tubular-shaped devices composed of complex patterns of interconnecting struts which function to hold open a segment of a blood vessel or other body lumen like oesophagus and urethra. Stent grafts are stents with a circumferential covering or lining and are suitable for supporting a dissected artery or intimal flap that can occlude a vessel lumen. Stents and stent grafts are typically implanted by use of a catheter. Initially they are maintained in a

radially compressed state to manoeuvre them through the lumen. Once in position, they are deployed. The material from which the vascular prosthesis like stents or stent grafts is constructed must allow the prosthesis to undergo expansion, which typically requires substantial deformation. Once expanded the stent must maintain its size and shape and must be capable of withstanding the structural loads, namely radial compressive forces, imposed on the stent as it supports the walls of a vessel lumen. The wall of the prosthesis must be sufficiently thick, depending on the stent material, not only to withstand the vessel wall recoil but also allow the stent to be seen on the fluoroscope. Finally, the prosthesis material must be biocompatible so as not to trigger any adverse vascular responses like restenosis or thrombus formation in the treated vessel.

For medical devices such as all kind of catheters and guide wires special mechanical properties are desired to have perfect trackability and pushability during the intervention. Moreover, good radio-opacity and MRI compatibility are essential in order to survey medical procedures via x-ray and MRI. Finally also for these medical devices biocompatibility is a must.

In the past years increased effort was undertaken to find new materials for medical implants and devices bearing superior characteristics over commonly used metals like stainless steel or titanium. Numerous publications focus on titanium alloys aiming at corrosion resistant, high strength and biocompatible alloys. As described for example in US 6,312,455, US 2001/0007953, and WO 99/58184 many Titanium-alloys thereof are super-elastic or shape memory alloys. A pseudo-elastic ß-titanium alloy fabricated from Titanium, Molybdenum, Aluminium and optionally Niobium, Chrome and Vanadium is described in US 6,258,182. EP 0 788 802 provides a self-expanding stent consisting of a titanium alloy including at least about 68 weight percent titanium and optionally Niobium, Zirconium, and Molybdenum. US 6,238,491 and WO 00/68448 describe a Niobium-Titanium-Zirconium-Molybdenum alloy for medical devices providing a uniform ß-structure, which is corrosion resistant, and can be processes to develop high-strength and low-modulus. The alloy comprises 29 to 70 weight percent Niobium, 10 to 46 weight percent Zirconium, 3 to 15 weight percent Molybdenum and a balance of Titanium. In another approach Davidson (EP 0 601 804) employ an alloy consisting essentially of Titanium, 10 to 20 or 25 to 50 weight percent Niobium and optionally up to 20 weight percent Zirconium, the alloy having an elastic modulus less than 90 GPa. Similar Titanium-alloys for medical implants also published by Davidson comprise Titanium, 10 to 20 or 35 to 50 weight percent Niobium and optionally up to 20 weight percent each Zirconium and Tantalum (EP 0 437 079) or Titanium, 10 to 20 or 35 to 50 weight percent each Niobium and

Tantalum and optionally up to 20 weight percent Zirconium (US 5,690,670). EP 0 707 085 also provides a low modulus, biocompatible Titanium-base alloy for medical devices consisting of 20 to 40 weight percent
Niobium, 4,5 to 25 weight percent Tantalum, 2,5 to 13 weight percent Zirconium and the balance Titanium. A further high strength, low modulus and biocompatible Titanium-alloy is laid open in US 4,857,269 and EP 0 359 446 consisting of Titanium and up to 25 weight percent Niobium, Zirconium, and Molybdenum. EP 1 046 722 describes a corrosion resistant Titanium-Zirconium-type alloy for medical appliances consisting of 25 to 50 weight percent Titanium, 5 to 30 weight percent Niobium, 5 to 40 weight percent Tantalum and 25 to 60 weight percent Zirconium.

Object of the Invention

It is an object of the present invention to provide medical implants or devices, especially stents which have favourable mechanical properties, excellent biocompatibility, good radio-opacity while at the same time exhibiting minor image artefact in MRI examination (MRI compatibility) and does therefore overcome the drawbacks of recently available metals for medical purposes.

The material should fulfil all mechanical and structural requirements according to its function in a medical implant or device. Moreover, the material should be sufficiently radio-opaque to allow for good imaging of the device under x-ray without the addition of an extra layer or portion of radio-opaque material. Also, the material should not overly bright in X-ray imaging and should not obscure the image of the surrounding tissue, as would be the case with a device made from an extremely dense material. In addition, the material should be MRI safe and compatible, preferably also visible under MRI.

Summary of the Invention

Surprisingly, it has been found that the desired properties can be given to a metal alloy essentially consisting of niobium and 0.85 to 1.15 % of zirconium.

Detailed Description of the Invention

The radio-opacity of the presently claimed Nb-Zr alloy is sufficient to be readily visualized under x-ray during medical procedures and yet is not so radio-opaque as to interfere with the visualization of surrounding body tissue.

The material is generally an alloy of about 99% of Zr, rest Nb (Nb-1%Zr or NbZr1) – known for long as a reactor tubing material and for various other applications. It can easily be obtained in sheet or tube form. It is especially suitable for stents which require delicate and complicated patterns to be cut from the sheet or tube. The cutting is usually done by laser methods. Stents with low wall thickness may conveniently be manufactured.

The alloy of the invention can be easily cold-worked to increase strength and reduce elastic modulus. It is possible to form a hard, abrasion resistant surface on the inventive alloy through standard oxidation and nitridizing methods known by those skilled in the art. The presence of a hard, inert, abrasion resistant surface layer presents an important option for medical implants and devices in which it is desirable to have lower friction and wear, electrical insulation and improved corrosion resistance.

To further improve the biocompatibility of the medical implant or device fabricated at least in part from the inventive alloy, at least a portion of the surface of the inventive alloy can be conversion surface hardened and/or coated. Such coatings can include, but are not limited to a polymer, a blend of polymers, a metal, a blend of metals, a ceramic and/or biomolecules, in particular peptides, proteins, lipids, carbohydrates and/or nucleic acids (e.g. collagen, heparin, fibrin, phosphorylcholine, cellulose, morphogenic proteins or peptides, growth factors). Furthermore the alloy surface or the coatings can comprise stem cells and/or a bioactive substances, in particular drugs, antibiotics, growth factors, anti-inflammatory agents and/or anti-thrombogenic agents. Further, the surface can be modified by electropolishing or mechanical polishing for formation of a completely smooth surface, sintering to achieve a porous coating as for example described in EP0601804, or by roughening procedures or microblasting, in particular sandblasting, to achieve a rough surface.

The Nb-Zr alloy is useful in the manufacturing of a variety of medical implants and devices. The manufacture of medical devices from the invention alloy includes minimal-invasive devices, in particular guide wires, catheters (balloon catheters, guiding catheter, angiographic catheters,

functional catheters), intra-cavernous implants, in particular intra-oesophagus, intra-urethra, intra-tracheal implants and intra-vascular implants, in particular stents, stent grafts, stent graft connector, heart valve repair device or filters.

The invention relates to medical implants or devices fabricated from the above-mentioned alloys, e.g.minimal-invasive devices, in particular catheters or guide wires, or intra-cavernous implants, in particular intravascular implants, such as stents, stent grafts, stent graft connectors or heart valve repair devices.

In the above implants and devices the surface of the metal alloys may be passivated by oxidation or nitridization, or may be electropolished, mechanically polished, micro blasted, roughened or sintered, or may be coated with a polymer, a blend of polymers, a metal, a blend of metals, a ceramic and/or biomolecules, in particular peptides, proteins, lipids, carbohydrates and/or nucleic acids; or may be coated with stem cells and/or a bioactive substance, in particular drugs, antibiotics, growth factors, anti-inflammatory agents and/or anti-thrombogenic agents.

A preferred material for the implants or devices of the invention is the following (All percentages are by weight): 98. 85 – 99.15 weight percent Niobium and 0.85 – 1.15 % Zirconium, preferably 99.05 – 99.15 weight percent Niobium, and 0.85 – 0.95 % weight percent Zirconium. Especially preferred is the material: 99.05 –99.15 weight percent Niobium and 0.85 – 0.95 % weight percent Zirconium.